Usher syndrome

Usher syndrome is a condition characterized by partial or total hearing loss and vision loss that worsens over time. The hearing loss is classified as sensorineural, which means that it is caused by abnormalities of the inner ear. The loss of vision is caused by an eye disease called retinitis pigmentosa (RP), which affects the layer of light-sensitive tissue at the back of the eye (the retina). Vision loss occurs as the light-sensing cells of the retina gradually deteriorate. Night vision loss begins first, followed by blind spots that develop in the side (peripheral) vision. Over time, these blind spots enlarge and merge to produce tunnel vision. In some cases, vision is further impaired by clouding of the lens of the eye (cataracts). However, many people with retinitis pigmentosa retain some central vision throughout their lives.

Researchers have identified three major types of Usher syndrome, designated as types I, II, and III. These types are distinguished by their severity and the age when signs and symptoms appear. The types are further divided into subtypes based on their genetic cause.

Most individuals with Usher syndrome type I are born with severe to profound hearing loss. Progressive vision loss caused by retinitis pigmentosa becomes apparent in childhood. This type of Usher syndrome also causes abnormalities of the vestibular system, which is the part of the inner ear that helps maintain the body's balance and orientation in space. As a result of the vestibular abnormalities, children with the condition have trouble with balance. They begin sitting independently and walking later than usual, and they may have difficulty riding a bicycle and playing certain sports.

Usher syndrome type II is characterized by hearing loss from birth and progressive vision loss that begins in adolescence or adulthood. The hearing loss associated with this form of Usher syndrome ranges from mild to severe and mainly affects the ability to hear high-frequency sounds. For example, it is difficult for affected individuals to hear high, soft speech sounds, such as those of the letters d and t. The degree of hearing loss varies within and among families with this condition, and it may become more severe over time. Unlike the other forms of Usher syndrome, type II is not associated with vestibular abnormalities that cause difficulties with balance.

People with Usher syndrome type III experience hearing loss and vision loss beginning somewhat later in life. Unlike the other forms of Usher syndrome, type III is usually associated with normal hearing at birth. Hearing loss typically begins during late childhood or adolescence, after the development of speech, and becomes more severe over time. By middle age, most affected individuals have profound hearing loss. Vision loss caused by retinitis pigmentosa also develops in late childhood or adolescence.

Some people with Usher syndrome type III have vestibular abnormalities that cause problems with balance.

Frequency

Usher syndrome is estimated to affect 4 to 5 per 100,000 people, although some studies suggest that the prevalence of the condition may be as high as 1 in 6,000 people. The condition is thought to account for 3 to 6 percent of all childhood deafness and about 50 percent of deaf-blindness in adults.

Types I and II are the most common forms of Usher syndrome in most countries. Type III represents only about 2 percent of all Usher syndrome cases overall. However, type III occurs more frequently in the Finnish population, where it accounts for about 40 percent of cases.

Genetic Changes

Usher syndrome can be caused by mutations in several different genes. Mutations in at least six genes can cause Usher syndrome type I. The most common of these are *MYO7A* gene mutations, followed by mutations in the *CDH23* gene. Usher syndrome type II can result from mutations in three genes; *USH2A* gene mutations account for most cases of type II. Usher syndrome type III is most often caused by mutations in the *CLRN1* gene.

The genes associated with Usher syndrome provide instructions for making proteins involved in normal hearing, balance, and vision. In the inner ear, these proteins are involved in the development and function of specialized cells called hair cells, which help to transmit sound and signals from the inner ear to the brain. In the retina, the proteins contribute to the maintenance of light-sensing cells called rod photoreceptors (which provide vision in low light) and cone photoreceptors (which provide color vision and vision in bright light). For some of the proteins related to Usher syndrome, their exact role in hearing, balance, and vision is unknown.

Most of the gene mutations responsible for Usher syndrome lead to a loss of hair cells in the inner ear and a gradual loss of rods and cones in the retina. Degeneration of these sensory cells causes the hearing loss, balance problems, and vision loss that occur with Usher syndrome.

In some people with Usher syndrome, the genetic cause of the condition has not been identified. Researchers suspect that several additional genes are probably associated with this disorder.

Inheritance Pattern

All of the types of Usher syndrome are inherited in an autosomal recessive pattern, which means both copies of a gene in each cell have a mutation. The parents of an

individual with Usher syndrome each carry one copy of the mutated gene, but they do not have any signs and symptoms of the condition.

Other Names for This Condition

- deafness-retinitis pigmentosa syndrome
- Graefe-Usher syndrome
- Hallgren syndrome
- retinitis pigmentosa-deafness syndrome
- Usher's syndrome

Diagnosis & Management

These resources address the diagnosis or management of Usher syndrome:

- GeneReview: Usher Syndrome Type I
  https://www.ncbi.nlm.nih.gov/books/NBK1265
- GeneReview: Usher Syndrome Type II
  https://www.ncbi.nlm.nih.gov/books/NBK1341
- Genetic Testing Registry: Usher syndrome type 2
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0339534/
- Genetic Testing Registry: Usher syndrome, type 1
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1568247/
- Genetic Testing Registry: Usher syndrome, type 3A
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1568248/
- MedlinePlus Encyclopedia: Retinitis Pigmentosa
  https://medlineplus.gov/ency/article/001029.htm

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Retinitis Pigmentosa
  https://medlineplus.gov/ency/article/001029.htm
- Health Topic: Hearing Disorders and Deafness
  https://medlineplus.gov/hearingdisordersanddeafness.html
- Health Topic: Hearing Problems in Children
  https://medlineplus.gov/hearingproblemsinchildren.html
- Health Topic: Retinal Disorders
  https://medlineplus.gov/retinaldisorders.html
- Health Topic: Usher Syndrome
  https://medlineplus.gov/ushersyndrome.html

Genetic and Rare Diseases Information Center

- Usher syndrome
  https://rarediseases.info.nih.gov/diseases/7843/usher-syndrome

Additional NIH Resources

- National Eye Institute
  https://nei.nih.gov/health/ushers/
- National Institute on Deafness and Other Communication Disorders
  https://www.nidcd.nih.gov/health/usher-syndrome
- National Institutes of Health
  https://ushersyndrome.nih.gov/

Educational Resources

- Boys Town National Research Hospital
  https://www.boystownhospital.org/research/molecularstudies/Pages/UsherSyndrome.aspx
- Centers for Disease Control and Prevention (CDC): Hearing Loss in Children
  https://www.cdc.gov/ncbddd/hearingloss/
- Cleveland Clinic
  http://my.clevelandclinic.org/health/articles/usher-syndrome
- Disease InfoSearch: Usher syndrome
  http://www.diseaseinfosearch.org/Usher+syndrome/7316

- Hereditary Hearing Loss Homepage: Clinical and Molecular Classification of Usher Syndrome
  http://hereditaryhearingloss.org/main.aspx?c=.HHH&n=86573
- MalaCards: usher syndrome
  http://www.malacards.org/card/usher_syndrome
- My46 Trait Profile
  https://www.my46.org/trait-document?trait=Usher%20syndrome&type=profile
- Nevada Dual Sensory Impairment Project, University of Nevada, Reno
  http://www.unr.edu/ndsip/
- Orphanet: Usher syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=886
- University of Virginia Health System
  https://uvahealth.com/services/eye-care/conditions-treatments/usher-syndrome

Patient Support and Advocacy Resources

- American Speech-Language-Hearing Association
  http://www.asha.org/Articles/Understanding-Usher-Syndrome/
- Foundation Fighting Blindness
  http://www.blindness.org/usher-syndrome
- Helen Keller National Center for Deaf-Blind Youths and Adults
  https://www.helenkeller.org/hknc
- Hope for Vision
  http://hopeforvision.org/
- National Center on Deaf-Blindness
  https://nationaldb.org/
- National Organization for Rare Disorders
  https://rarediseases.org/rare-diseases/usher-syndrome/
- Resource List from the University of Kansas Medical Center
  http://www.kumc.edu/gec/support/usher.html
- Usher III Initiative
  http://usheriii.org/
- Usher Syndrome Coalition
  https://www.usher-syndrome.org/
- Usher Syndrome Registry
  https://www.usher-registry.org/

GeneReviews

- Usher Syndrome Type I
  https://www.ncbi.nlm.nih.gov/books/NBK1265
- Usher Syndrome Type II
  https://www.ncbi.nlm.nih.gov/books/NBK1341

Genetic Testing Registry

- Retinitis pigmentosa-deafness syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0271097/
- Usher syndrome type 2
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0339534/
- Usher syndrome type 2c, GPR98/PDZD digenic
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C3148929/
- Usher syndrome type ID/F, CDH23/PCDH15, digenic
  https://www.ncbi.nlm.nih.gov/gtr/conditions/CN121478/
- Usher syndrome, type 1
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1568247/
- Usher syndrome, type 1B
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1848638/
- Usher syndrome, type 1C
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1848604/
- Usher syndrome, type 1D
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1832845/
- Usher syndrome, type 1E
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1865865/
- Usher syndrome, type 1F
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1865885/
- Usher syndrome, type 1G
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1847089/
- Usher syndrome, type 1H
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C2675458/
- Usher syndrome, type 1J
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C3553944/
- Usher syndrome, type 1K
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C3539124/

- Usher syndrome, type 2A
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1848634/
- Usher syndrome, type 2C
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1854237/
- Usher syndrome, type 2D
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1568249/
- Usher syndrome, type 3A
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1568248/
- Usher syndrome, type 3B
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C3281066/

ACT Sheets

- Congenital hearing loss >~30db
  https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/Hearing_Loss.pdf

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Usher+syndrome%22

Scientific articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Usher+Syndromes%5BMAJR%5D%29+AND+%28usher+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM

- USHER SYNDROME, TYPE I
  http://omim.org/entry/276900
- USHER SYNDROME, TYPE IC
  http://omim.org/entry/276904
- USHER SYNDROME, TYPE ID
  http://omim.org/entry/601067
- USHER SYNDROME, TYPE IE
  http://omim.org/entry/602097
- USHER SYNDROME, TYPE IF
  http://omim.org/entry/602083
- USHER SYNDROME, TYPE IG
  http://omim.org/entry/606943

- USHER SYNDROME, TYPE IH
  http://omim.org/entry/612632
- USHER SYNDROME, TYPE IIA
  http://omim.org/entry/276901
- USHER SYNDROME, TYPE IIC
  http://omim.org/entry/605472
- USHER SYNDROME, TYPE IID
  http://omim.org/entry/611383
- USHER SYNDROME, TYPE IIIA
  http://omim.org/entry/276902
- USHER SYNDROME, TYPE IIIB
  http://omim.org/entry/614504
- USHER SYNDROME, TYPE IJ
  http://omim.org/entry/614869
- USHER SYNDROME, TYPE IK
  http://omim.org/entry/614990

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  https://www.ncbi.nlm.nih.gov/books/NBK1265
- GeneReview: Usher Syndrome Type II
  https://www.ncbi.nlm.nih.gov/books/NBK1341
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